12 25X1A

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CENTRAL INTELLIGENCE AGENCY

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25X1A 25X1X

SUPPLEMENT TO REPORT NO. [redacted]

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25X1A

1. With respect to the new anti-biotic and the substance to increase the activities of various anti-biotics developed by Ivan Villax, mentioned in [redacted] the attachment describes both these substances as closely as possibly without exactly revealing their origin and manner of production.

25X1A

2. This anti-biotic produced from onions is not identical with an extract discovered by a Soviet scientist, under the name "phytoncides". It is alleged that only certain types of onions can be used for the production of anti-biotics.

Attachments: 1 report on anti-biotic research

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ATTACHMENT I

A. Nature of anti-biotic extract from onions (E).

I. Fatty-type of compound. It disintegrates beyond 100° Centigrade; is constant at room temperature.

II. Experimental data in vitro:

1. The results of the official experiments of the National Institute for Health (Orszagos Közegeszségügi Intezet, Budapest, Gyali ut 4-6) are as follows:

a. E used on E coli has the same activity as Streptomycin.

b. 1 mg of E corresponds to about 950 Oxford units of Staphylococcus aureus (standard Oxford strain). 1 mg of penicillin (corresponds to) 1650 Oxford units.

2. E was also tested on the following bacteria: Pneumococcus, Para-typhus, Typhus B (limit of dilution beyond 1:1,000,000) also Streptococcus pyogenes, B. pyocyaneus, Sarcina lutea, B. antracoides, B. Fluorescens liquefaciens, Proteus X-19, pseudo tuberculosis Rodentium (limit of dilution between 1:100,000 - 1:1,000,000).

III. Experimental data in vivo:

1. Toxicity with regard to mice:

Intravenous injection:

0.2 g/kg	mild agitation, fast breathing
0.75 g/kg	temporary depression, lowering of temperature
1.20 g/kg	severe depression, lowering of temperature
1.48 g/kg	death within one minute

Intraperitoneal injection:

0.4 g/kg	mild agitation, fast respiration
1.6 g/kg	paralysis of the nerve center, lasting for hours, lowering of temperature (reversible)
2.0 g/kg	death after 1.5 hours
2.5 g/kg	death after an hour

Administered orally:

0.3 g/kg	no reaction
5.0 g/kg	mild depression, after slight agitation, lasting 1-2 hours

2. Pharmacological experiments:

Local effect:

0.25 g	no subcutaneous reaction
0.20 g	the place of injection is slightly swollen after 24 hours

25X1A

Effect on blood pressure of cats drugged with urethane:

0.006 - 0.03 g/kg intravenous	no effect
0.53 g/kg intravenous	marked but short-lasting lowering of blood pressure

The Dreser apparatus was used to measure the effect of respiration of rabbits who had not been drugged:

0.5 g/kg intravenous	for a short time the respiration rate increased by 40-50% and the volume per minute of breath is increased by 20%. This amount causes Bradycardia and a lowering of the temperature to 33° Centigrade, and marked depression. The toxic symptoms decrease after 2 hours and disappear after 12 hours.

Effect on isolated frog hearts:

Dilution:	
1:1,000	no reaction
1:200 - 1:300	negative isotrop effect (spontaneous reversible)
1:100	paralyzes the heart but reversible after flushing
1:200	was ineffective with respect to creating and maintaining irritation

3. Animal experiments in experimental injections in rabbits. E injected at the same time when the animals were inoculated with pseudo-tuberculosis Rodentium (Daranyi's method): the bacteria produced no effect. With Staphylococcus aureus and E. coli injections in every stage of illness the daily 3/4 mg subcutaneous E-doses during 16-36 hours produced symptoms.

4. Dr. E.N. Modrovich, Magyarovar, and others carried out clinical experiments. With 32 different E. coli infections a daily dosis of 5x6 mg given orally was sufficient to obtain prompt cure after 12 - 60 hours. With 46 influenza cases 4x10 mg E administered subcutaneously daily was sufficient for cure. With six cases of Endocarditis lenta disappearance of fever was accomplished within 6-8 days with 5x30 mg E daily. After 3-4 weeks the bacteriological test was negative. E was also effective in Staphylococcus, typhus, and other infections.

B. Nature of substance (S) which has capability to increase the activity of various anti-biotics many times.

I. S is a plant extract: crystallizable, hygroscopic compound. Its action does not decrease and it remains constant at room temperature. It begins to deteriorate at 70° Centigrade and at 100° Centigrade it deteriorates completely.

II. Experimental data in vitro: In the experiments, a preparation of Merck & Co., Rahway, was used which contained 600-605 mg of Streptomycin (STR) and a Hungarian dosis (of the Palik firm) of 525 mg of Streptomycin (STR). The STR-doses given below have therefore been converted to a pure STR-base.

1. Method of dilution. Ordinary clear soup was used as nutritive solution; it was incoculated with an intermediate culture of Staphylococcus aureus lasting 24 hours. (0.1 ml intermediate culture and 3.9 ml nutritive solution and 1.0 ml S and STR solution.) Incubation temperature was 37° Centigrade.

25X1A

STR/ml	S/ml	Bacteria growth 24 hours	48 hours
4	-	slight turbidity	turbidity
6	-	-	slight turbidity
6.6	-	-	-
-	950	-	-
-	900	slight turbidity	turbidity
4	4	-	-
2	2	-	-
1	1	-	slight turbidity
1.2	1.2	-	-

Experimentation on E coli in addition to the above-listed conditions:

STR/ml	4	5	5.5	4	2	1.5	1.25	1	1	1.25
S/ml	-	-	-	4	2	1.5	1.25	1	2	0.625
18 hours										slight turbidity
21 hours										
24 hours										

2. The cylinder method produced the same results: and 1 S and 1 STR mixture produced about four times greater activity with regard to E coli cultures than the same amount of STR alone With regard to other bacteria (Streptococcus haemolyticus and pyogenes, pneumococcus, proteus vulgaris, pseudo tuberculosis Rodentium, etc.) a similar effect can be observed. Furthermore, S is effectively combined with other anti-biotics.

III. Experimental Data in Vivo:

1. Toxicity: S has practically no toxic effect. Lethal dose is 1.4-1.6g/kg intravenous; with regard to mice, the dosis depends on its purity. The toxicity of STR does not increase when mixed with S.

2. Clinical experiments were directed by Dr. E. N. Modrovich, Magyarovar, but the tests could not be completed, A fine partial result was obtained in tuberculosis therapy: the combination of STR and S was considerably more effective than STR alone Production costs are very low, approximately 1500-2000 Swiss francs per kilogram.